Pergamon

Tetrahedron Letters, Vol. 38, No. 50, pp. 8745-8748, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)10341-0

Indium in Organic Synthesis: Convenient Synthesis of β,γ-Unsaturated Ketones.

J.S. Yadav*, Dale Srinivas, Gondi Sudershan Reddy and Konuru Hima Bindu.

Indian Institute of Chemical Technology, Hyderabad-500 007, India.

Abstract: A mild and efficient method for the preparation of β,γ unsaturated ketones by a simple reaction on acid chloride with allyl, crotyl, prenyl bromide and indium in DMF is described.

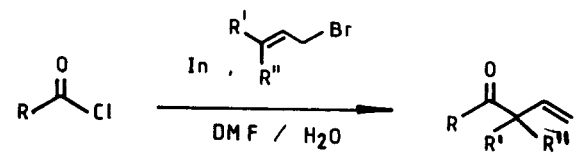
Synthesis of β,γ unsaturated ketones is complicated by the inherent liability of the double bond towards prototropic rearrangement producing conjugated isomeric α,β unsaturated ketones.[1] Although deconjugation of α,β unsaturated ketones can be achieved by a variety of methods,[2] mixtures of α,β and β,γ unsaturated isomers are often produced. Thus the reaction conditions need to be as mild as possible. Even though a number of synthetic methods are available only a few have been proven useful and practical.[3] Acylation of olefins frequently favours the production of β,γ-unsaturated ketones, but α,β-unsaturated ketones may also be generated. Certain transition metal mediated syntheses have been partially successful, but they also suffer from pure regiospecificity. Claisen rearrangement of α-alkoxy ketone enol derivatives provide β,γ unsaturated ketones with good selectivity but the procedure is tedious.[4] Among other methods, direct oxidation of homoallylic alcohols produced via allyl boration have been demonstrated to be successful for specific classes.[5] Homoallylic ketones have also been prepared by the reaction of allylic organometallics of silicon,[6] mercury,[7] zinc,[8] copper,[9] titanium,[10] tin,[11] manganese,[12] rhodium[13] and cadmium[14] with acyl halides, but these reactions are of limited application since they are not simple and straight forward. In addition some of these procedures entail the problems of corrosivity and effluent pollution. In view of the synthetic importance of β,γ unsaturated ketones, it is desirable to have a general and convenient methodology for their synthesis especially from readily available materials.

Herein we wish to disclose a mild, efficient and convenient method for the synthesis of various homoallylic ketones through allylation of acid chlorides using allyl, crotyl and prenyl bromides and indium[15]

I.I.C.T. Communication No. 3849

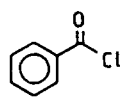
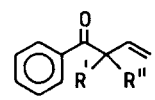
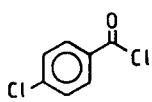
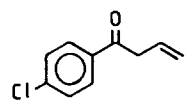
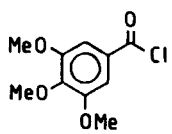
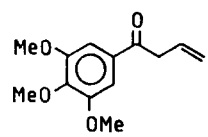
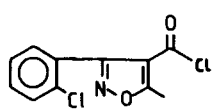
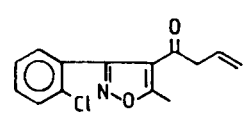
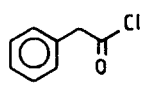
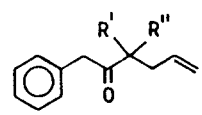
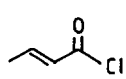
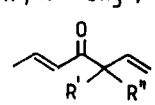
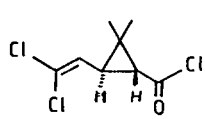
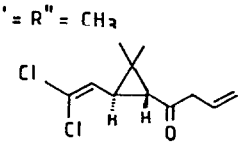
in DMF at room temperature. (Scheme I)

Scheme-1



In a typical case indium metal powder (1 mmol) was added to a stirred solution of allyl bromide

Table

Entry	Starting material	Product	Yield%
1		 R'=R" = H , R' = H , R" = CH_3	80 - 85
2			82
3			72
4			68
5		 R' = H , R" = CH_3 , R' = R" = CH_3	75 - 85
6		 R' = R" = H , R' = H , R" = CH_3 R' = R" = CH_3	55 - 70
7			65 - 82

(1 mmol) in 3-5 ml of DMF and the stirring was continued for 30 min. at room temperature. Freshly distilled acid chloride (1 mmol) was then added dropwise and the progress of the reaction was monitored by tlc. After 3 hrs the reaction mixture was quenched with a few drops of water and the product was isolated by extraction with CH_2Cl_2. Purification by column chromatography on silica gel gave homoallylic ketone in 80-90% yields exclusively and there was no evidence for the formation of isomeric conjugated α,β unsaturated ketone. When crotyl bromide was used in place of allyl bromide in the above reaction the β,γ unsaturated ketone (entry 1,5,6) was obtained in 70-85% yield without the formation of any α,β unsaturated ketone. Similar treatment of other acid chlorides gave the corresponding β,γ unsaturated ketones in 70- 90 % yields and typical examples are summarised in the table. All the compounds obtained were characterised by IR and ^1H NMR spectroscopy and finally by comparison with authentic samples.

In conclusion the present procedure for the synthesis of β,γ unsaturated ketones provides much improvement over the existing methods and makes a useful and important addition to the present methodologies. The main advantages of this new method are mild reaction conditions, tolerance to the olefinic double bond, no prototropic isomerisation during the reaction and excellent yields.

Acknowledgements: Authors (Dale Srinivas, Gondi Sudershan Reddy) to C.S.I.R and (Konuru Himabindu) to U.G.C. are thankful for financial support in the form of a Fellowship.

References:

1. a) Rehman A.U. *Studies in Natural Products* Vol 1-8. b) Cardillo, G.; Simone, A.D.; Mingardi, A.; Tomasini, C. *Synlett,* **1995**, 1131-1132. (References cited therein). c) Demuth, M.; Mikhail, G. *Synthesis* **1989**, 145-162.

2. a) Groves, J.K. *Chem Soc. Rev.* **1972**, *1*, 73-97. b) Noyce, D.S.; Evett, M. *J. Org. Chem.* **1972**, *37*, 394-397. (c) Aumiller, J.C.; Whittle, J.A. *J. Org. Chem.* **1976**, *41*, 2959-2962.

3. (a) Monti, S.A.; White, G.L. *J. Org. Chem.* **1975**, *40*, 215-217. (b). Hoffman, H.M.R.; Tsushima, T. *J. Am. Chem. Soc.* **1977**, *99*, 6008-6011. (c) Beak, P.; Berger, K.R. *J. Am. Chem. Soc.* **1980**, *102*, 3848-3856. (d) Earnshaw. C.; Torr, R.S.; Warren, S. *J. Chem. Soc. Perkin Trans. 1.* **1983**, 2893-2901.

4. Kachinsky, J.L.C.; Salomon, R.G. *J. Org. Chem.* **1986**, *51*, 1393-1401.

5. Zaidlewicz, M. *Synthesis* **1988**, 701-703.

6. (a). Hosomi, A.; Hashimoto, H.; Sakurai, H. *J. Org. Chem.* **1978**, *43*, 2551-2552. (b). Laguerre, M.;

Dunogues, J.; Calas, R. *Tetrahedron Lett.* **1980**, *21*, 831-834. (c). Hayashi, T.; Konishi, M.; Ito, H.; Kumuda, M. *J. Am. Chem. Soc.* **1982**. *104*, 4962-4963.

7. Larock, R.C.; Lu, Y. *J. Org. Chem.* **1993**, *58*, 2846-2850.
8. (a) Ranu, B.C.; Majee, A.; Das, A.R. *Tetrahedron Lett.* **1996**, *36*, 4885-4888. (b) Ranu, B.C.; Majee, A.; Das, A.R. *Tetrahedron Lett.* **1996**, *37*, 1109-1112.
9. Sato, T.; Kawara, T.; Nishizawa, A.; Fujisawa, T; *Tetrahedron Lett.* **1980**, *21*, 3377-3380.
10. Kasatkin, A.N.; Kulak, A.N.; Tolstikov, G.A. *J. Organomet. Chem.* **1988**, *346*, 23-24.
11. Labadie, J.W.; Tueting, D.; Stille, J.K. *J. Org. Chem.* **1983**, *48*, 4634-4642.
12. Cahiez, G.; Laboue, B. *Tetrahedron Lett.* **1989**, *30*, 7369-7372.
13. Hegedus, L.S.; Kendall, P.M.; Lo, S.M.; Sheats, J.R. *J. Am. Chem. Soc.* **1975**, *97*, 5448-5452.
14. Sandhu, J.S.; Baruah, B.; Boruah, A.; Prajapati, D. *Tetrahedron Lett.* **1996**, *37*, 9087-9088.
15. a) Araki, S.; Ito, H.; Butsugan, Y. *J. Org.Chem.* **1988**, *53*, 1833-1834. b) Chao, L.C.; Rieke, R.D. *J. Org. Chem.* **1975**, *40*, 2253-2255. c) Araki, S.; Butsugan, Y.; *J.Chem. Soc. Chem. Commun.* **1989**, 1286-1287. d) Araki, S.; Katsumura, N.; Kawasaki, K. I.; Butsugan, Y. *J. Chem. Soc. Perkin Trans 1,* **1991**, 499-500. e) Araki, S.; Shimizu, T.; Johar, P. S.; Jin, S. J.; Butsugan, Y. *J.Org. Chem.* **1991**, *56*, 2538-2542. f) Araki, S.; Butsugan, Y. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 727-729. g) Araki, S.; Shimizu, T.; Jin, S. J.; Butsugan, Y. *J. Chem. Soc. Chem. Commun.* **1991**, 824-825. h) Araki, S.; Ito, H.; Katsumura, N.; Butsugan, Y. *J.Organometallic Chem.* **1989**, *369*, 291-296. i) Araki, S.; Katsumura, N.; Ito, H.; Butsugan, Y. *Tetrahedron Lett.* **1989**, *30*, 1581-1582. j) Araki, S.; Katsumura, N.; Butsugan, Y. *J.Organometallic Chem.* **1991**, 415, 7-24. k) Beuchet, P.; Le Marrec, N.; Mosset, P. *Tetrahedron Lett.* **1992**, *33*, 5959-5960. l) Li, C.J.; Chan, T.H. *Tetrahedron Lett* **1991**, *32*, 7017-7020. m) Grée, D.; Grée, R.; Lowinger, T.B.; Martelli, J.; Negri, J.T.; Paquette, L.A. *J. Am. Chem. Soc.* **1992**, *114*, 8841-8846.

(*Received in UK* 22 *July* 1997; *revised* 3 *October* 1997; *accepted* 10 *October* 1997)